AMENDMENT OF NIAID SOLICITATION
"In vitro and Animal Models for Emerging Diseases and Biodefense"

Solicitation Number:	RFP NIH-NIAID-DMID-03-39
Amendment Number:	Three (3)
Amendment Issue Date:	Wednesday, January 22, 2003
Proposal Intent Response Sheet Due Date:	Monday, December 30, 2002
Proposal Due Date: (UNCHANGED)	**Tuesday, February 4, 2003 at 4:00 PM Local Time**
Issued By:	Paul D. McFarlane Senior Contracting Officer NIAID, NIH, DHHS Contract Management Branch, DEA 6700-B Rockledge Drive Room 2230, MSC 7612 Bethesda, Maryland 20892-7612
Point of Contact:	Paul D. McFarlane, Contracting Officer E-Mail: pm24v@nih.gov

This amendment is issued to all potential Offerors.

The above numbered solicitation is amended as set forth below. The hour and date specified for receipt of proposals **HAS NOT BEEN EXTENDED**. Offerors must acknowledge receipt of this and all other amendments, by identifying this amendment number (and any others) on each copy of any offer(s) submitted. Failure to receive your acknowledgement may result in the rejection of your offer. If, by virtue of this amendment, you wish to change an offer already submitted, such changes may be made by telegram, letter or e-mail, provided each telegram, letter or e-mail makes reference to this solicitation amendment number and is received prior to the opening hour and date specified. Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full force and effect.

PURPOSE OF AMENDMENT: This amendment revises the Generic Part C Statement of Work, revises the instructions for preparation, packaging and delivery of Generic and Task Order proposals, reduces and defines the content of the Generic and Task Order proposals, and allows Offerors to decide the term of performance for any Task Order Proposals submitted.

1. Under the RFP section titled, BACKGROUND/STATEMENT OF WORK/NOTES TO OFFERORS, STATEMENT OF WORK, PART C: SMALL ANIMAL MODELS FOR SELECTED PATHOGENS INCLUDING GLP STUDIES, the generic Part C statement of work (SOW) is hereby revised to allow studies using animal models infected with botulinum toxin. Therefore, this pathogen has been removed from the first paragraph of the SOW as it was listed in the main RFP and in Amendment #2, dated January 15, 2003. (Although the rest of the SOW is unchanged, it is provided in its entirety so it may be read in context with the first paragraph as amended.)

PART C: SMALL ANIMAL MODELS FOR SELECTED PATHOGENS INCLUDING GLP STUDIES

The third activity area to be supported under this contract is the development, validation and use of various small animal models to screen new therapeutic, diagnostic and preventive agents or test the efficacy of therapeutics, immunotherapies, diagnostics, and vaccines with activity against emerging infectious agents including, Bioterrorism Category A-C agents. These contracts will provide a ready capacity in a number of needed areas and be utilized, as products become available for testing. Other studies such as disease pathogenesis and natural history are not intended for this contract. In vivo safety testing, pharmacokinetics, pharmacodynamics, and toxicity testing are covered under Part E and F of this solicitation. Models for testing of Rift Valley Fever vaccine, Plague vaccine, and screening of currently licensed and marketed antibiotics for anthrax and pneumonic plague are a priority for the NIAID. Offerors are also encouraged to propose models for other important emerging and/or rare viral and bacterial agents as well. Not intended for this solicitation, are animal models for infection with Variola major (human smallpox), Filoviruses, and Viral Hemorrhagic Fever agents specifically: Punta Toro, Pichinde, Benzi, and Semlicki Forest viruses, TB, and Influenza.

Independently, and not as an agent of the government, the Contractor shall develop small animal models to be used for screening and efficacy testing of new products including therapeutics, immunotherapies, diagnostics, and vaccines. Conduct all in vivo testing as are required for approval of a product for human administration. Testing must be sufficient to meet requirements for Investigational New Drug (IND) filing.

Specifically, as directed by the Project Officer, the contractor shall:

1. Utilize or provide one or more well-characterized and validated animal models(s) of human infection and/or disease mediated by Category A-C disease agents to evaluate candidate diagnostics, drugs, vaccines and immunotherapies for preliminary efficacy. (A validated model is one that has shown correlation of results with human clinical trials or trials conducted in Non-Human Primates (NHP) or with the natural history of human infection and is suitable to provide data relevant for obtaining FDA approval for an IND, licensure, or specific indication. The Project Officer will provide guidance for these models.) For infection models, the infection of animals should be efficiently established. For other models, for example, mice transgenic with the human virus receptor gene or mice implanted with virus-infected human tissues, provide and use animals for evaluation of candidate therapies. For all models, the process and dosage level of infection and challenge and/or disease pathogenesis should resemble the corresponding human disease as closely as possible. Standardized protocols, when provided by the Project Officer, shall be incorporated.

2. Perform pre-clinical evaluations of experimental therapies, diagnostic, and preventive agents for infections as specified by the Project Officer. The test agents shall be evaluated for efficacy. When appropriate, conduct studies to evaluate novel strategies for drug delivery and dosing, including combination and sequential drug administration. These studies shall include appropriate uninfected and untreated controls and may involve aerosol challenge of some agents requiring specialized testing facilities. Federal guidelines for care and use of laboratory animals must be followed as well as requirements for approval of animal use protocols. Unless directed otherwise, submit each proposed protocol/experiment/effort to the Project Officer for review, prioritization, and approval. The NIAID Project Officer will provide agents for evaluation. Some, but not all studies will require that they be performed in accordance with Good Laboratory Practice (GLP) regulations. Evaluation capabilities of the animal model shall include, but not be limited to, the following:
a. Quantitative assessments, which detect differences, with at least a minimal level of statistical confidence, between treatment groups of animals, with specific indicators including confirmation of infection, quantitation of organisms present in tissues of infected animals, markers of disease progression, and selected indicators of morbidity.
b. Microbiological and histological analyses, including but not limited to special stains and cultures, to document the purity, severity, pathology, and location of the animal infection. Necropsy/pathology support shall be available as needed.
c. Appropriate observations and measures of general toxicity, to include body weight, blood chemistries, hematologic measures, body temperature, behavior, and other indicators of general health.
d. Immunogenicity and/or immune responses when appropriate for the test article.
e. Limited pharmacokinetic determinations. Offerors will be required only to have the capability of collecting and preparing blood, cell, and tissue samples for shipment to another site for analysis.

3. Perform further studies to characterize and refine the proposed model(s) and to develop new models. The contractor may be required, as directed by the Project Officer, to use animal models other than the one proposed if well-characterized animal models become available. As directed by the Project Officer, develop and evaluate new assays and models that may be required for new/emerging agents and models.

4. Conduct work with animals in accordance with NIH guidelines for animal care and use. Maintain awareness of evolving regulatory requirements for animal research and with the FDA regulatory guidelines for animal studies in support of licensure, such as the 21 CFR Parts 314 and 601 “New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical of Feasible.” When efficacy studies are intended to support the clinical use of a test article in humans, the contractor shall also:
a. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.
b. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.
c. Maintain awareness of evolving regulatory requirements for preclinical toxicologic evaluations for chemicals or biologics, and develop new test systems or models as required to meet new needs.
d. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

2. In the solicitation, under Section J, the portion entitled, How to Prepare and Submit an Electronic Proposal, is amended to read as follows:

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL WITH PAPER ORIGINALS - PAGE LIMITS

For this solicitation, it has been decided that Offerors are NOT required to submit any proposals to the NIAID Internet site. Therefore, Offerors will not need any log-in or password information to access this site. However, Offerors are required to create electronic copies of their proposals and to provide these on either a ZIP DISKETTE or a COMPACT DISK (CD) with their paper proposal submissions. Please carefully read and follow the directions below for preparing and submitting proposals.

For the Generic proposals there is a 200 PAGE LIMITATION for the Technical Proposal portion, inclusive of appendices, attachments, operating manual excerpts, letters of intent, any non-electronic data, etc. Pages in excess of this limitation will be removed from the Generic Proposal(s) and will NOT be read or evaluated. In determining whether or not to include any technical proposal content, consider whether or not you believe the NIAID will need the information in order to make a complete evaluation of the proposal(s). Non-electronic data means any information provided with your proposal that is ONLY available in a paper version. Clearly identify these portions by listing them, with an asterisk and a key thereto, in the Table of Contents of your technical proposal(s). Note that Offerors' Generic technical proposals are to be submitted in hard (paper) copy in an original and thirty (30) copies. Offerors must create two (2) separate electronic files (one containing the technical proposal and one containing the business proposal FOR EACH GENERIC PROPOSAL) and shall convert these to PDF format and submit them on either a ZIP DISKETTE or a COMPACT DISK (CD) with their paper originals and copies. Example: If you submit a proposal under one Generic Part, the diskette or CD should contain two separate files, 1 technical proposal file and 1 business proposal file for that Generic Part, in addition to the number of Task Order proposals below.

For the Task Order proposals there is a 150 PAGE LIMITATION for the Technical Proposal portion, inclusive of appendices, attachments, operating manual excerpts, letters of intent, any non-electronic data, etc. Pages in excess of this limitation will be removed from the Task Order Proposal(s) and will NOT be read or evaluated. In determining whether or not to include any technical proposal content, consider whether or not you believe the NIAID will need the information in order to make a complete evaluation of the proposal(s). Non-electronic data means any information provided with your proposal that is ONLY available in a paper version. Clearly identify these portions by listing them, with an asterisk and a key thereto, in the Table of Contents of your technical proposal(s). Note that Offerors' Task Order technical proposals are to be submitted in hard (paper) copy in an original and thirty (30) copies. Offerors must create two (2) separate electronic files (one containing the technical proposal and one containing the business proposal FOR EACH TASK ORDER PROPOSAL) and shall convert these to PDF format and submit them on either a ZIP DISKETTE or a COMPACT DISK (CD) with their paper originals and copies. Example: If you submit two Task Order Proposals under one Generic Part, the diskette or CD should contain six separate files (i.e. 1 technical proposal and 1business proposal for the first Task and 1 technical proposal and 1 business proposal for the second Task, plus the 1 technical and 1business proposal for the Generic Part to which these two tasks pertain.)

INSTRUCTIONS FOR CONTENT AND DELIVERY OF BUSINESS PROPOSALS

Note that although there is no page limitation for the Business Proposals, (for either the generic or task order business proposals) Offerors are encouraged to limit their size and content to only those documents necessary to provide adequate support for the proposed costs. To save redundant copying and including of resumes with multiple Generic and Task Order proposals, Offerors are encouraged to provide one (1) complete set of resumes for all staff proposed (for their institution and for each subcontractor). These resumes should be limited to 2-page bio-sketches that identify the individual, their experience and any publications specific to this acquisition. (The NIAID Contracting Officer will provide these resume sets to the scientific review group.)

For purposes of this solicitation, Offerors need ONLY submit a Small Business Subcontracting Plan as part of the original Generic Business Proposal(s). Hence, there is no need to provide a separate Small Business Subcontracting Plan for any Task Order proposals submitted for this solicitation. This Plan will be negotiated prior to any awards under this requirement. Further, Offerors are ONLY REQUIRED TO SUBMIT ONE (1) COPY EACH of their institution's most recent Annual Financial Report, Travel Policy (if applicable), and completed Representations and Certifications. These should also be provided with the original Generic Business Proposal(s). Offerors are only required to submit an original and five (5) copies of their Generic and Task Order Business Proposals. The NIAID Contracting Officer will provide the necessary cost information from these business proposals to the scientific review group.

3. Amendment #2, dated January 15, 2003 mandated that Offerors build three (3) year budgets for each Task Order they propose. It has since been determined this three (3) year period is not mandatory. Instead, Offerors may build budgets for their individual Task Orders, for less than or greater than 3 years (but no greater than seven years), depending upon their expertise and knowledge about how long any Task should take to complete. NIAID reserves the right to negotiate each of these task order budget proposals prior to making any awards under this requirement.

END OF MODIFICATION #3 TO RFP NIH-NIAID-DMID-03-39